

In the Claims:

Please cancel claims 1-33 and add the following new claims 34-70 before calculating the application filing fee:

34. A matrix for forming a skeletal joint comprising articular cartilage and bone at a defect site in a mammal, the matrix comprising:

a biocompatible support material including bone and associated articular cartilage tissues having dimensions and structural relationships to each other which correspond anatomically to those of the skeletal joint to be replaced, and, disposed on the surfaces of said matrix,

substantially pure osteogenic protein in an amount sufficient to induce formation of new said bone and associated articular cartilage thereby to permit regeneration of said skeletal joint at said defect site.

35. The matrix of claim 34 further comprising a carrier associated with osteogenic protein disposed on or in said matrix.

36. A method of replacing a defective skeletal joint comprising the steps of:

- a) excising said defective skeletal joint; and
- b) implanting the matrix of claim 34 or 35 at the site of excision.

37. The method of claim 36 comprising the additional step of implanting a muscle flap.

38. The matrix of claim 34 wherein said osteogenic protein is selected from the group consisting of: OP-1, OP-2, BMP5, BMP6, BMP2, BMP4, BMP9, DPP, Vg-1, 60A, Vgr-1, including naturally sourced and recombinant derivatives of the foregoing.

39. The matrix of claim 34 wherein said osteogenic protein is selected from the group consisting of: OP-1, OP-2, BMP2, BMP3, BMP4, BMP5, BMP6, including naturally sourced and recombinant derivatives of the foregoing.

40. The matrix of claim 34 wherein said osteogenic protein is OP-1 or a related osteogenic protein.

41. The matrix of claim 34 further comprising support material selected from the group consisting of ligament, tendon, joint capsule, menisci, intervertebral discs, and synovial membrane tissue.

42. The matrix of claim 34 wherein said support material comprises anterior cruciate ligament.

43. The matrix of claim 34 wherein said support material comprises a functional attachment site of tendon or ligament to bone.

44. The matrix of claim 34 wherein said support material comprises fibrovascular tissue.

45. A device for repair of a skeletal joint defect in a mammal which serves as a template to form in vivo a functional replacement skeletal joint comprising plural distinct tissues, the device comprising:

- a) a biocompatible matrix defining a unitary intact structure allowing the attachment of infiltrating cells, said matrix comprising plural distinct tissues including at least one non-mineralized tissue of a joint and including bone and having dimensions and shape conforming to the skeletal joint to be repaired; and disposed on the surface of said matrix,
- b) an osteogenic protein in an amount sufficient to induce formation of new said plural distinct tissues, thereby to permit regeneration of a replacement skeletal joint comprising plural distinct tissues, wherein said osteogenic protein comprises a 6- or 7-cysteine skeleton at the C-terminal end.

46. The device of claim 45 wherein said matrix comprises anterior cruciate ligament.

47. The device of claim 45 wherein the matrix comprises fibrovascular tissue.

48. The device of claim 45 wherein said matrix comprises a functional attachment site of tendon or ligament to bone.

49. A device for implantation in a mammal which serves as a template for forming in vivo articular cartilage replacement tissue, the device comprising:

exogenous osteogenic protein disposed on the surface of a biocompatible matrix,

said matrix comprising plural distinct tissues including articular cartilage, said tissues defining a unitary structure which allows the attachment of infiltrating cells thereby to permit regeneration of said articular cartilage in a skeletal joint, wherein said exogenous osteogenic protein is selected from the group consisting of OP-1, OP-2, BMP5, BMP6, BMP2, BMP4, BMP9, DPP, Vg-1, 60A, Vgr-1.

50. A device for implantation in a mammal which serves as a template for forming in vivo replacement non-mineralized tissue, the device comprising:

osteogenic protein disposed on the surface of a biocompatible matrix,

said matrix comprising plural distinct tissues including at least one non-mineralized tissue corresponding in kind to said tissue to be replaced, said matrix defining a unitary structure which allows the attachment of infiltrating cells thereby to permit regeneration of non-mineralized tissue in a skeletal joint, wherein said exogenous osteogenic protein is selected from the group consisting of OP-1, OP-2, BMP5, BMP6, BMP2, BMP4, BMP9, DPP, Vg-1, 60A, Vgr-1.

51. The device of claim 49 or 50 wherein said matrix comprises fibrovascular tissue.

52. The device of claim 49 or 50 wherein said matrix comprises anterior cruciate ligament.

53. The device of claim 49 or 50 wherein said matrix comprises a functional attachment site of tendon or ligament to bone.

54. A method for inducing in a mammal the formation of a replacement skeletal joint, said method comprises the steps of:

a) providing a device comprising osteogenic protein and plural distinct tissues including at least one non-mineralized tissue of a joint and including bone, and,

having dimensions and shape which conform to the skeletal joint to be replaced; and

b) implanting said device at a locus in mammal, thereby to induce formation of a functional replacement skeletal joint comprising plural distinct tissues.

55. A method for repairing in a mammal an articular cartilage defect, the method comprising the step of:

providing to said defect in a mammal a device comprising an osteogenic protein disposed on the surface of a biocompatible matrix, wherein said osteogenic protein is selected from the group consisting of OP-1, OP-2, BMP5, BMP6, BMP2, BMP4, BMP9, DPP, Vg-1, 60A, ^{and} Vgr-1, said matrix comprising plural distinct tissues, said tissues defining a structure which allows the attachment of infiltrating cells thereby to permit regeneration of articular cartilage in a skeletal joint.

56. A method for repairing in a mammal a non-mineralized tissue defect in a skeletal joint, the method comprising the step of:

providing to said defect a device comprising osteogenic protein disposed on the surface of a biocompatible matrix, wherein said osteogenic protein is selected from the group consisting of OP-1, OP-2, BMP5, BMP6, BMP2, BMP4, BMP9, DPP, Vg-1, 60A, Vgr-1, said matrix comprising plural distinct tissues including at least one non-mineralized tissue to be replaced, said matrix defining a structure which allows the attachment of infiltrating cells thereby to permit regeneration of non-mineralized tissue in a skeletal joint.

57. The method of claim 54, 55 or 56 wherein said matrix comprises anterior cruciate ligament.

58. The method of claim 54, 55 or 56 wherein said matrix comprises fibrovascular tissue.

59. The method of claim 54, 55 or 56 wherein said matrix comprises a attachment site of tendon or ligament to bone.

60. The method of claim 54, 55 or 56 wherein said device further comprises collagen, polymers comprising lactic acid, butyric glycolic acid or mixtures thereof; hydroxyapatite and combinations thereof.

61. A device for forming an articulating skeletal joint at a defect site in a mammal, the device comprising:

a biocompatible matrix comprising

an articulating surface, and,

plural distinct tissues including at least one non-mineralized tissue, said tissues having dimensions and structural relationships to each other which correspond anatomically to the articulating skeletal joint to be replace, and, disposed on or within said matrix,

substantially pure osteogenic protein in an amount sufficient to induce formation of an articulating surface and plural distinct tissues thereby to permit regeneration of said articulating skeletal joint at said defect site.

62. A device for forming plural distinct non-mineralized tissues in an articulating skeletal joint, the device comprising:

a biocompatible matrix comprising,

an articulating surface, and,

plural distinct non-mineralized tissues having dimensions and structural relationships to each other which correspond anatomically to the articulating skeletal joint to be replaced, and, disposed on or within said matrix,

substantially pure osteogenic protein in an amount sufficient to induce formation of a new articulating surface and new plural distinct non-mineralized tissues thereby to permit regeneration of said articulating skeletal joint at said defect site.

63. The device of claim 61 or 62 wherein said non-mineralized skeletal joint tissue comprises anterior cruciate ligament.

64. The device of claim 61 or 62 wherein said non-mineralized skeletal joint comprises fibrovascular tissue.

65. The device of claim 61 or 62 wherein at least one of said non-mineralized skeletal joint tissue comprises a functional attachment site of tendon or ligament to bone.

66. The device of claim 61 or 62 wherein said exogenous osteogenic protein comprises homodimers or heterodimers of OP-1, OP-2, BMP2, BMP3, BMP4, BMP5, BMP6, OPX, BMP9, DPP, Vg-1, Vgr-1 and 60A or naturally sourced and recombinant derivatives of the foregoing.

67. The device of claim 61 or 62 wherein said matrix is devitalized.

68. The device of claim 61 or 62 wherein the osteogenic protein comprises a 6 or 7 cysteine skeleton in the C-terminal region.

69. The matrix of claim 34 wherein the osteogenic protein comprises a 6 or 7 cysteine skeleton in the C-terminal region.

70. The method of claim 54, 55 or 56 wherein the osteogenic protein comprises a 6 or 7 cysteine skeleton in the C-terminal region.

REMARKS

Claims 1-33 have been canceled and new claims 34-70 have been added. Upon entry of this paper, claims 34-70 will be pending in this application.

Applicants have amended the specification on page 1 to correct related patent information.